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PATHOGENIC ACTION OF THE ATMOSPHERE

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Sostoyaniy [Pathological Physiology of Extreme Conditions],
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16. Abstract

The effects of variation atmospheric pressure (hypobaria, hyperbaria) on various parts of the living organism are examined at length. Separate treatment is devoted to the role of low partial oxygen pressure and to hyperoxia primarily in the production of pathological phenomena.

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PATHOGENIC ACTION OF THE ATMOSPHERE

N. N. Sirotinin[1]

Over a long period of development, living organisms have been accustomed   /36*
to an atmospheric pressure which we call normal (760 mm Hg). For a number of
species, for example abyssal forms, normal pressure is several times greater
than this value; on the other hand, for inhabitants of high altitude locations
the value is much less. We do not know exactly what the atmosphere was like
during previous geological epochs; it may be assumed that it varied in its
density and qualitative composition. There was a time when there was a great
deal more carbon dioxide than there is now, and less oxygen. The atmosphere
has not undergone significant changes since man appeared.

Although the concept of atmospheric pressure apparently arose long ago,
its precise measurement only became possible when Torricelli (1643) measured
atmospheric pressure by means of the mercury barometer. It was found that
variations in barometric pressure from normal by 10-20 mm Hg do not cause any
pathological phenomena in healthy human beings. It was noticed a long time
ago, however, that persons of advanced age, suffering from rheumatism, can
sense a slight drop in pressure, suffering pain in the joints. At the present
time, considerable material has been gathered (D. Assman, 1966; D. I. Panchenko,
Yu. A. Isakov, L. P. Lukashevich, 1964) which indicates that there is an in-
fluence of a pressure decrease on patients with a wide variety of ailments. An
analysis of these diseases shows that they consist primarily of allergic ail-
ments or diseases with an allergic component| (Quinke's edema, bronchial asthma,
myocardial infarct, etc.). It has frequently been observed that such pathologi-
cal symptoms can precede a change in barometric pressure; however, they could
not be produced under pressure-chamber conditions. On the basis of this and
other factors, we can assume that these phenomena are related to other
meteorological factors which accompany a drop in barometric pressure.

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The influence of barometric pressure on blood circulation was considered in a study of the problem of the active diastole of the heart, or its suction power (A. Fokht, 1917). A. A. Bogomolets (1929, 1940) laid great importance on this fact. He wrote that atmospheric pressure is the motive force which is /37 responsible for the transfer of the blood from the capillaries into the right auricle, like a siphon. He suggested that atmospheric pressure could limit high-altitude flights. But this view was expressed prior to flights up to the ceiling for unpressurized cabins. Donati (1934), in the course of such a flight, reached an altitude of 14,435 meters (atmospheric pressure 99 mm Hg, partial pressure of oxygen 12 mm Hg). In 1936, using oxygen apparatus, V. V. Kokkinaki made an ascent to 14,575 meters. Approximately the same drop in atmospheric pressure was withstood in a pressure chamber by various researchers who breathed oxygen. In particular, N. N. Sirotinin reached an "altitude" of 14,500 meters in a pressure chamber. This shows that reaching high altitudes limits the drop not only in atmospheric but also partial pressure of oxygen, which leads to acute hypoxic hypoxia. With a rapid drop in atmospheric pressure in a pressure chamber, when it is not possible for hypoxia to develop, even higher animals can withstand a much greater drop in barometric pressure than that mentioned above for a short period of time.

Hypobaria

The first experiments to explain the influence of hypobaria on the living organism were performed by Torricelli, but they were incomplete and constituted a source of error in themselves. The beginning of classical studies in this area were marked by Boyle (1670) who showed beyond a doubt that a sharp drop in atmospheric pressure caused animals to die when gas bubbles formed in their blood vessels; he observed such bubbles in the aqueous humor of the eye in a snake which was in a container from which the air had been pumped. Later, a similar series of experiments was performed on various animals by various authors who added nothing substantially new.

It was only beginning with Bert (1878) that classical data on hypobaria were obtained. This author collected a large volume of material on the effect of reduced barometric pressure on representatives of various animal species and showed that hypobaria produces its effect primarily through reduced partial

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oxygen pressure. Breathing the latter prevents the development of many pathological symptoms. Prior to these studies of hypobaria, great emphasis was placed on the pathogenesis of the pathological processes that are observed when atmospheric pressure drops. Thus, even hyperemia of the skin, mucous membranes and various types of hemorrhages were linked to this factor. Bert's viewpoint was developed by V. V. Pashutin (1881) and others.

A drop in atmospheric pressure by several millimeters usually has no effect on higher animals, but fish which live in deep water feel it because of the distention of the air bladder as they arise. In the past, such fish as loaches and chars were used instead of barometers. We know that when abyssal fishes are brought up rapidly, the air bladder is forced out through the mouth.

Low hypobaria influences the human organism only when the atmospheric pressure drops rapidly; this influences the pressure of the gases in closed spaces and in cavities that communicate with the external air, through compressible openings. The tympanic cavity and inner ear are particularly sensitive in this regard. This is explained by the considerable flexibility of the eardrum in response to small variations in barometric pressure. The tympanic cavity communicates through the Eustachian tube with the nasopharynx, equalizing the pressure between this cavity and the surrounding atmosphere; blockage /38 of the Eustachian tube by mucus increases sensitivity to changes in barometric pressure; this is usually felt when making an ascent in an aircraft. Swallowing movements promote the equalization of pressure and eliminate the unpleasant sensation.

To a lesser degree, hypobaria influences the accessory sinuses of the nose and the frontal sinuses. According to the data of A. P. Popov (1938), a painful sensation is usually felt in the sinuses when ascending to an altitude of 3,000-4,000 meters (526-462 mm Hg). A. D. Gurkov (1940), studying this problem in experiments on animals, found that when the atmospheric pressure drops in a pressure chamber, hyperemia, hemorrhaging, dilation of the lymph channels in the mucous and submucous membranes are observed in cats and dogs. However, this occurs at comparatively high atmospheric rarefactions, and both hypobaria and hypoxia are involved in the pathogenesis of these pathological processes.

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We know that when the atmospheric pressure drops the functional ability of the eye is disrupted; however, the breathing of oxygen restores it partially or completely. The latter indicates that disturbance of function is dependent primarily upon hypoxia and not upon hypobaria; however, the influence of the latter has been insufficiently studied. Armstrong (1949) writes that in pilots over 40 the most frequent change affecting the eye is presbyopia, which is encountered even in young pilots. N. N. Sirotinin observed in himself that almost daily sessions in a pressure chamber at reduced atmospheric pressure caused progressive presbyopia; suspension of these autoexperiments slowed its onset. However, we still do not know what role is played in this phenomenon by hypobaria and the extent to which hypoxia is involved.

The pressure in the pleural cavity varies within narrow limits as a function of inspiration and expiration. Hypobaria causes an increase in the pressure in this cavity, although it levels off rapidly when gas is breathed.

A normal stomach contains a small amount of air whose pressure does not exceed 4-5 cm water column. In the event of rapid hypobaria, this air expands and is expelled through the mouth with regurgitation.

Even Bert (1878) noticed that dilation of the intestine was one of the constantly observed symptoms of hypobaria. A. N. Kruglyy (1833-1934) showed that at an altitude of 5,000-7,000 meters (405-308 mm Hg) the periodic activity of the stomach and intestine slackened. M. P. Brestkin found inhibition of the secretory function of the stomach at reduced barometric pressure (cited in V. V. Strel'tsov, 1938). However, this evidently involves hypoxia more than hypobaria.

A study of the therapeutic effects of hypobaria has also been carried out. Bert (1878) names three French physicists as pioneers in this area: Junod, Tabarie and Pravaz. It should be pointed out that this method began to be used soon afterward by A. O. Katolinskiy (1862). However, his method of carrying out experiments was such that the action of the rarefied atmosphere amounted primarily to hypoxia. At the present time, hypobaria is used in the clinic in the form of a local limited action in the form of application of cups to the skin.

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Bert (1878) studied hypobaria in a pressure chamber at various pressure levels, up to 120 mm Hg, on various species of animals. With pronounced and rapid rarefaction, he observed explosion of the air bladder in fish, as well as dilation and rupture of the lungs and stomach in frogs. In dogs, he observed a pronounced dilation of the stomach; the animals rapidly died from asphyxia. We have already mentioned that even before Bert, Boyle and others /39 noticed development of gas bubbles during pronounced atmospheric rarefaction, which led to emboli in the vessels of various organs. Many authors have studied the consequences of hypobaria in the form of decompression.

It has been established that the harmful effects of hypobaria depend upon both the degree and rapidity of its development; the faster and more pronounced the hypobaria, the more pronounced its pathological symptoms. The most serious consequences are the gas bubbles, composed primarily of nitrogen, which separate from the tissues. This phenomenon is subject to considerable individual variations. It was noticed a long time ago that obese persons can withstand pronounced hypobaria worse than those who are slender; this is explained by the fact that the fat in the tissues at normal body temperature can dissolve 5 to 6 times more nitrogen per unit mass than the blood (Vernon, 1917), so that more nitrogen accumulates in the blood of obese persons. The nitrogen bubbles enter the vessels and are transported by the blood to various parts of the organism, causing emboli in the vessels. They may combine to form large bubbles; this frequently occurs in the spaces of the heart and causes reduced propulsive force or even cessation of function.

The emboli are particularly dangerous when they affect the coronary vessels; emboli of the pulmonary vessels are less dangerous but can lead to hemorrhages, partial emphysema, and pulmonary edema. Embolism affecting the vessels of the abdominal cavity is not felt subjectively (Armstrong, 1954), but may cause severe hemorrhaging (N. N. Sirotinin, V. D. Yankovskiy, Yu. F. Gerya, 1969). Embolism of the vessels of the central nervous system is a dangerous symptom. The emboli frequently observed in the vessels of the pia mater are not so dangerous.

The development of pathological phenomena, particularly emboli, is a function of the rate of rarefaction of the atmosphere. According to the data

of Armstrong (1954), there are still no experimental studies that can be used as a basis for determining the maximum permissible rate of development of hypo-baria at which the formation of gas bubbles will not occur. According to theoretical calculations, gas bubbles will develop if rarefaction takes place at a rate in excess of 2.25 mm/minute (ascent at the rate of 23 m/minute). With "ascent" in a pressure chamber to an "altitude" of 5,400 meters (rare-faction to 379.4 mm Hg), no symptoms of embolism develop at all, but at an "altitude" of 9,000 meters (225.6 mm Hg) symptoms of decompression disease may develop. These are not permanent and differ markedly as a function of the individual; they are most markedly evident in middle-aged persons. According to the data of Gray and Masland (1946), moderate physical stress causes earlier development of decompression symptoms. Data are available which indicate that at an altitude of 3,000 to 5,400 meters pains may develop at the site of old bone fractures and other injuries to the joints and muscles. Armstrong (1954) suggests that these depend not so much on the development of gas bubbles as on certain other factors of unknown etiology which cause these same phenomena when the weather changes.

Pathological phenomena in hypobaria, taking the form of decompression disease, have been studied by a great many authors both in the Soviet Union and abroad.

A great many of these studies have been devoted to an examination of the mechanism of bubble formation -- "boiling". On the basis of theoretical calculations, this has been found to occur at 47 mm Hg, i.e., at an altitude of approximately 19,000 meters.

External symptoms of gas accumulation take the form of inflation of ani-mals, as has been observed in rabbits, rats, dogs and particularly well in frogs. In addition, it is possible to observe the development of bubbles in the saliva and blood. N. N. Sirotinin, V. D. Yankovskiy and Yu. F. Gerya (1969) observed these phenomena in dogs with cannulae inserted in the cervical vessels. They also observed "boiling" of the urine which was excreted. Other authors performed highly demonstrative studies by passing the blood of animals through a chamber with double, thin glass walls; they placed the animals in a pressure chamber where the atmosphere was rarefied. At an "altitude" of approximately

17,600 meters (57.7 mm Hg), bubbles could be seen with the naked eye which formed more rapidly with further "ascent". At an "altitude" of approximately 19,000 meters (46.18 mm Hg) a "soap bubble" picture developed.

The study of the chemical composition of the air in these bubbles revealed that they contained primarily nitrogen as well as water vapor, carbon dioxide and small amounts of oxygen. According to the data of Ye. A. Kovalenko and Yu. A. Yurkov (1961, 1962), during the first 10 seconds the bubbles contained primarily nitrogen, with the amount reaching 73.37%, as well as oxygen and carbon dioxide; the amount of carbon dioxide was 10.57%. By the 20th second, the amount of carbon dioxide had risen to 34.12%. By the 40-50th second it reached 66.11% and the nitrogen content dropped to 22.75%. Kovalenko feels that the amount of oxygen in the blood at high altitudes increases due to its excretion from the tissues; it later decreases and the oxygen content in the bubbles drops (from 16.06 to 11.32%).

An important role in the development of these bubbles is played by the time of their formation and the rate of elimination of nitrogen through the lungs from the organism. Burchardt, Adler, Thometz, Atkinson and Ivy (1946) "lifted" seven subjects to an "altitude" of 10,860 meters (170.6 mm Hg) and kept them at this altitude, breathing oxygen, for two hours. By means of x-ray photographs it was established that under these conditions the gas bubbles appeared within 5 to 10 minutes.

Reducing the time of hypobaria, it is possible to "ascend" to high "altitudes". Thus, Luft (1950), by breathing oxygen, was able to spend 10 seconds at a pressure of 46.58 mm Hg; he felt no symptoms indicating "boiling". The rate of elimination of nitrogen during hypobaria has been studied by many authors (A. P. Apollonov, L. L. Shik, 1941, Stevens, Pyder, Ferris, Inatoma, 1947; Behnke, Thomson, Shaw, 1935; Margaria, Sendroy, 1950; Gillespie, 1952). It has been demonstrated that nitrogen excretion during hypobaria is initially increased and drops off later on.

Explosive decompression. Armstrong (1954) found decompression disease to be a complex of symptoms that is primarily a consequence of the excretion of gas bubbles into the tissues and fluids of the organism; this in turn is the consequence of exposure to hypobaric conditions. However, as has already been

observed earlier, a certain period of time is required for the gas bubbles to appear; on this basis, it may be assumed that gas embolism is related to hypobaria but develops after a slight delay. Explosive decompression can be of the delayed or rapid variety. Armstrong produced explosive decompression corresponding to its equivalent (1,500 meters/minute) by discharging gas from a chamber with a volume of 1 m^3 through an opening with a diameter of 14 mm^2. Violette (1961) feels that decompression can be considered explosive if two conditions are present: a coefficient of escape of more than 1/100 m^2/m^3 and a pressure ratio above 2.3.

Decompression can be produced in various ways. Retarded decompression is obtained by means of a powerful vacuum pump and a pressure chamber volume which is as small as possible. Explosive decompression of the rapid variety occurs when a small chamber containing animals is connected with a large chamber in /41 which the atmospheric pressure has been markedly reduced.

The effects of explosive decompression on the organism have much in common with the effects of hypobaria, but all of the phenomena develop more rapidly. Thus, subcutaneous emphysema with decompression to 30 mm Hg begins to develop after 30-40 seconds (Edelmann, Hitchcock, 1948 and others). Studies of a gas bubble during explosive decompression to 30-25 mm Hg within 0.02 second showed that it contains water vapor, carbon dioxide, nitrogen and oxygen (Beman, Kampf, 1948; I. S. Balakhovskiy, 1956; A. G. Kuznetsov, 1957; Ye. A. Kovalenko, Yu. A. Yurkov, 1961 and others).

The effect of explosive decompression has been studied in the human organism, particularly in the form of autoexperiments. Luft (1950) and later Hornberger (1950) studied the effect of rapid decompression on themselves at "altitudes" of 19,000 meters (46.58 mm Hg). When they breathed oxygen, they were able to remain under these conditions for up to 10 seconds without losing consciousness. N. A. Agadzhanyan, M. I. Vokar, A. R. Mansurov and A. S. Tsivilashvili (1958) studied the development of emphysema in the unprotected hand in 15 men. Out of 100 ascents, emphysema developed in 28 cases after 5-10 minutes of exposure to an altitude above 20,000 meters. P. N. Ivanov, A. G. Kuznetsov, V. B. Malkin and Ye. O. Popova (1960) performed 27 such studies involving hypobaria at the 41-8.5 mm Hg level; in 38 instances they

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observed the development of subcutaneous emphysema in the hand; this did not cause any deterioration of the individual's condition, but painful sensations were felt after 3-5 minutes.

The majority of studies involving explosive decompression have been performed on rats, rabbits and dogs. To a certain degree, these studies reveal the comparative pathology of this extremal state. More detailed comparative-pathological studies were performed by I. M. Khazen et al. (1969). These authors found that laboratory mice, subjected to a pressure drop from 760 to 40 mm Hg, almost all died; 15% of the rats subjected to the same effect survived; guinea pigs were still more resistant, followed by the rabbits. Dogs in Khazen's experiments turned out to be more resistant to explosive decompression than the rodents; cats were more resistant still. Monkeys and human beings proved to be most resistant. I. M. Khazen (1969) explains the evolution of such resistance to explosive decompression by the development of compensatory "devices" in the course of evolution.

Comparative-pathological studies were carried out on a broader basis by V. Ya. Lukhanin (1970). He performed experiments on representatives of the protozoa, coelenterata, worms, mollusks, arthropods (crustaceans and insects), fish, amphibians, reptiles, as well as representatives of the classes of birds and mammals. Lukhanin found that invertebrates were distinguished by a high level of resistance to explosive decompression.

Homoiothermal animals in general were slightly less resistant to rapid hypobaria than poikilothermal animals. Small birds (sparrows) with intensive metabolism show low resistance; even at 20 mm Hg they begin to die within 15 seconds. Laboratory mice in the experiments of V. Ya. Lukhanin, as well as in the experiments of I. M. Khazen, showed themselves to be less resistant than rats. Cats and dogs can survive hypobaria to 30-40 mm Hg for no more than 2 minutes (A. G. Kuznetsov, 1957). N. N. Sirotinin, V. D. Yankovskiy and Yu. F. Gerya (1969) also noted survival of dogs (particularly puppies) during this period of time and at lower pressure.

Comparative-pathological data show that death following rapid decompression /42 is independent of hypobaria. V. Ya. Lukhanin (1970) reports that with a leakage coefficient of 2.6 m^2/m^3 and 0.16 m^2/m^3 in their experiments, all animals

survived when recompression to the original level was performed immediately after the final pressure level was reached. Their literature contains reports of sudden death from explosive decompression which the authors explain by shock, the "battering ram effect" of the gases as a result of tissue emphysema, but not hypobaria itself. However, it has not been possible to establish a direct relationship between the degree of subcutaneous emphysema and tolerance to rapid hypobaria. According to the data of A. G. Kuznetsov (1957), the most extensive emphysema is observed in animals with a well-developed subcutaneous cell structure, for example rabbits, which are more resistant to rapid hypobaria than mice, with a less developed subcutaneous cell structure. However, still greater subcutaneous emphysema is observed in frogs, which possess very high resistance to rapid hypobaria. Gas embolism frequently plays a role in the lethal outcome, but is not of critical significance.

V. Ya. Lukhanin (1970), on the basis of his own data, like other authors concluded that the principal factor in mortality in rapid hypobaria is anoxia. If we compare the results of comparative-pathological studies on hypobaria with similar ones for hypoxia, we can see much in common (see page /50). The resistance in hypobaria, as in hypoxia, is greater in less-organized animals than in higher organisms.

This data indicates the possibility of reanimation in the event of clinical death from rapid hypobaria. N. N. Sirotinin, V. D. Yankovskiy and Yu. F. Gerya (1966, 1969) attempted to revive 37 dogs which had suffered clinical death from decompression to 30-14 mm Hg, lasting from 10-20 minutes. They managed to restore cardiac activity in 12 dogs and to restore breathing for several hours to several days. Of these animals, four remained alive for a long period of time without any visible defects. The author suggests that the unsuccessful attempts at reanimation were defeated by emboli in the vessels of the heart and brain, and therefore suggests that prior to reanimation the atmospheric pressure should be brought to a level of 2 atm above the original level; the air should then be replaced by oxygen.

Hyperbaria

The animal organism normally is exposed to hyperbaria at great depths in water.

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When descending in water, the pressure rises 1 atmosphere every 10.3 meters. At deep places in the ocean (9,640 meters) life goes on at a pressure of 1,000 atmospheres. Such pressures cannot exist at the surface of the Earth under natural conditions, since air is 770 times lighter than water and even the deepest shafts do not exceed 100 meters. Life is possible at the bottom of the greatest deeps. Microbes can withstand a pressure of 3,000 atm, retain total viability and grow on nutrient media (G. Tamman and G. Khlopin; cited in G. V. Khlopin, 1930). At the present time, it is possible to develop much greater pressures artificially: protozoa will remain alive even at pressures in excess of 10,000 atm. At depths studied by the "Vityaz" expedition in the Pacific Ocean (10,960, 10,816, 10,382 and 10,002 meters), there were a great many new species, genera and even families of animals. Among them, those of particular interest include the pogonophera -- long invertebrates like worms, /43 devoid of a digestive canal, which in the opinion of A. V. Ivanov constitute a completely new group of animals (Ye. M. Kreps, 1959). Some mollusks, such as *Lepidoptheurus benthus*, live at quite considerable depths (4,200 meters).

Pathological phenomena are produced both by hyperbaria and the gradient of its variations. Thus, in the larval and adult forms of crustaceans, plankton, etc., when the hydrostatic pressure rises, there is an increase in locomotion ("barokinesia"[1]). In shrimps, an increase in pressure by 50 atm (approximately 500 meters) causes temporary barokinesia, while a pressure of 150 atm has a paralytic effect. Other invertebrates -- coelenterata, ctenophora, echinoderms, mollusks -- are less sensitive to a change in pressure (Kinne, 1964). The "Vityaz" expedition established that polychaeta, cephalopoda and lamellibranchiate mollusks are found at a depth of 6,000 meters.

The acrania, which live on the sea bottom, are subjected to rather high pressure, particularly the family Amphioxididae, genus Amphioxides, which are found in the ocean.

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[1]Barokinesia in crustaceans in shallow water evidently is a function namely not of an increase in atmospheric pressure but a slight hypoxia in the subjacent layers of water, since these animals are sensitive to a rapid development of oxygen insufficiency. This explains the paralytic effect on them at great depths.

The great depths of the Atlantic Ocean are inhabited primarily by invertebrates; fish are rarely found. We know that poikilothermal vertebrates can withstand pronounced increases in atmospheric pressure and dive to great depths. Turtles are helped in this regard by their shells, which prevent significant compression of the chest. Some diving forms of animals, which descend to great depths, have special accommodations for withstanding hydrostatic pressure. Thus, the whales and seals (*Bullae osseae*) have skulls with very thick walls, lungs with dense walls of pulmonary parenchyma, and cartiledge around the small bronchi. This makes it possible to withstand high ambient pressure while holding the breath. Creating an air reserve in this fashion, these animals can descend to great depths for a comparatively long time: the cachalot for 1.5 to 2 hours, the Greenland whale for 1 hour, seals and beavers for 15 minutes, man for 2.5 minutes or, after basic training, for 3-4 minutes (cited in Ye. M. Kreps, 1941; Prosser, Braun, 1967).

Longer stays under water are limited not by pressure but by shortage of oxygen. The maximum depths that can be reached by homoiothermal animals vary for different species. Aquatic and diving birds, beavers, walruses and seals can dive 30-40 meters, whales can reach 100 meters and the cachalot can even go down several hundred meters. Thus, the body of a cachalot was found tangled in a cable on the bottom of the Atlantic Ocean at a depth of 900 meters.

The fundamental study of the effects of increased atmospheric pressure was begun by Bert (1878), who presented data on the effects of increased atmospheric pressure on various species of animals, from low forms to man. The author showed that the pathological phenomena were primarily linked to the toxic effects of oxygen under pressure. The studies of Bert remained unsurpassed for a number of years. Later works (Regnard, 1891; Basset, 1927; /44 Ebbecke, 1936; cited in N. V. Lazarev, 1941) are of interest in the sense that their authors used much higher pressure levels, taking the hydrostatic pressure into account. They confirmed Bert's data and also presented new facts. Thus, it was found that viruses are characterized by a high resistance to hyperbaria; tobacco mosaic virus can withstand 9,000 atm or more; it is inactivated only when exposed to this pressure for at least 1-2 days. The state of the organism is of great significance as far as resistance to hyperbaria is concerned. In

the active state, bacteria will die at an average of 6,000 atm, while spores can withstand a pressure of even 20,000 atm. According to the data of Fontaine (1930), the cells of higher animals undergo irreversible changes at 700 atm. Ebbecke (1935) reported that subjecting muscles to omnidirectional pressure in a special chamber at 800 atm causes them to contract, accompanied by a reversible loss of the pattern.

Hyperbaria in the work of divers and caisson workers. An untrained individual can be submerged in water for about 1 minute; further stay under water is limited by accumulation of carbonic acid and shortage of oxygen. Training consists of holding the breath and increasing the oxygen supply; under such conditions a man can remain under water for 3-4 minutes and dive to a depth of 30 meters or more. The hydrostatic pressure to which such a diver is subjected is 3 atm and does not cause serious disruption to the organism. Divers wearing diving suits can be subjected to much greater pressure.

A flexible diving suit makes it possible to go down to a depth of 60-80 meters with air being pumped through a hose from the surface. In the early 1930's, the record depths for the ventilated type of equipment were 100-110 meters. Further descent in water was limited by the toxic effects of oxygen (see the section entitled "Hyperoxia"), which can be eliminated by using a mixture that is low in oxygen, and also by the narcotic effect of compressed nitrogen (N. V. Lazarev, 1941). The latter can be eliminated by replacing the nitrogen by helium (N. V. Lazarev, 1941; A. P. Brestkin, P. M. Gramenitskiy and N. Ya. Sidorov, 1964; G. L. Zal'tsman and I. D. Sinov'yeva, 1964 and so forth).

As a result of various improvements, it has now been possible for a man wearing a diving suit to descend to still greater depths. Quite recently, the maximum depths were 100-150 meters, then 150-200 meters for periods up to 1 hour or more (Ye. M. Kreps, 1941). Then they increased further, although according to Lanphier (1964), as of 1962 no one had yet gone down to a depth of more than 300 meters (30 absolute atmospheres).

Table 8 shows the obstacles to deep dives in a flexible diving suit and methods of overcoming them (N. V. Lazarev, 1941).

TABLE 8

Depth (in m)	Obstacle	Method of Overcoming it
5 and more	Pain in the ears, damage and rupture of the eardrums due to incomplete equalization of pressure on the inside and outside.	Preliminary check of the patency of the Eustachian tubes. Training in the ability to facilitate equalization of pressure in the middle ear and the outside.
more than 13	Decompression diseases following ascent and emergence on the surface.	Carrying out a special procedure involving decompression, breathing oxygen during descent, and sometimes "on the ground", using a helium-oxygen mixture. The most improved method is mixed administration of gas mixtures, for example nitrogen-oxygen and helium-oxygen.
20-30	Initial signs of "nitrogen intoxication".	
90-100	Severe symptoms of "Nitrogen intoxication".	Alternate administration of gases -- weakest narcotics (helium and oxygen).
100-150	Loss of consciousness due to the narcotic action of the nitrogen.	
90-100	Stimulating effect of oxygen on the lungs.	Decrease in percentile composition of oxygen in the inspired gas mixture supplied to the diver.
140-190	General oxygen poisoning, nausea[1].	Ditto.
300-400	Narcotic effect of helium and hydrogen (?).	Antinarcotic substances (?).
500-600	Narcotic effect of helium and hydrogen. Mechanical effects of pressure.	Unknown.
More than 500-600 (how much more, not clear).	Zone of absolute intolerance.	None.

[1]During descent in oxygen insulating devices, observed at much shallower depths.

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In Table 8, the effect of hydrogen at depths of 300-400 meters is followed by a question mark. Further studies have shown that the addition of hydrogen to a gas mixture does not enable monkeys to withstand a descent to a depth of 600 meters.

Thus, the limiting pressure for man still remains 30 atmospheres. The white mouse can survive for a short time at a pressure of 100 atm in an environment composed primarily of indifferent gases (N. V. Lazarev, 1941). Obviously this value is close to the limit for terrestrial vertebrate animals. Ebbeke et al., observed noticeable changes in the central nervous system in a frog submerged in water under these conditions.

The use of rigid diving suits has facilitated work under water because the walls of the diving suit withstand the hydrostatic pressure and the patho-   /45 logical phenomena associated primarily with the partial pressure of the gas mixture which is used. It is clear from Table 8 that this is the primary limiting factor. In a bathysphere (spherical steel chamber), it is possible to descend to a depth of 900 meters; the steel walls of this device can withstand the hydrostatic pressure, and the atmospheric pressure inside it can be set as desired. Piccard descended in his bathyscaphe to the bottom of the Marianas Trench (10,387 meters).

A caisson is a waterproof structure for working under water or in wet soil; when it is used, a work area is created in which it is possible to carry out work at various depths by means of compressed air. Initially caissons were made in the shape of large boxes, thus giving rise to this name, originally French in origin. At the present time, they come in different shapes and, together with the compressor units and other auxiliary equipment, make up an   /46 entire assembly (Ye. V. Platonov, 1932).

Work in caissons, as in diving suits, is divided into three periods: the initial period (compression) extends from the beginning of descent to the reaching of the maximum depth; the second period involves work at maximum depths or "on the bottom"; the third period is the ascent or return to the surface -- decompression. Changes in atmospheric pressure occur during the first and third periods.

Gamel' (1820) observed that he felt pain in his ears when he dived into water; he correctly related these to insufficient patency of the eustachian tube. This phenomenon has been mentioned repeatedly in the literature thereafter. Pain in the ears occurs first at a depth of 2-3 meters and becomes more intense later on. It can be reduced by swallowing and may even disappear; this is due to improvement of the patency of the eustachian tube. At a depth of 6-7 meters, the pain is very severe and sometimes intolerable; this serves as a signal to ascend. If this is not done, barotrauma will develop; the pain will vanish as a result of rupture of the eardrum, frequently leading to a sensation of warmth associated with hemorrhaging. Hemorrhaging from the ears while working under pressure may not be a consequence of increased external pressure. In the majority of cases, only hyperemia of the eardrum is observed, which can lead to ecchymoses, as well as hemorrhages in them (K. L. Khilov, 1923; R. A. Zasosov, 1927; S. L. Rips, A. S. Putilov, 1940, and others).

In order to prevent such barotraumas, for the purpose of equalizing the pressure in the middle ear cavity and the external pressure, the diver is brought up 1 to 1.5 meters and then allowed to descend again. If this does not help, the descent is terminated. Usually the diver descends at the rate of 10 meters/minute. If no pathological phenomena develop, descent can proceed more rapidly (10-15 meters/minute). Painful sensations also arise in the accessory sinuses of the nose, but to a lesser degree. All of these phenomena usually occur at shallow depths and are independent of both the pressure as such and the rate at which it increases. The respiration rate slows down as the pressure rises and the depth of inspiration increases; inspiration is facilitated but expiration is slowed by hyperbaria; pulmonary ventilation is unaffected. The pulse rate slows down; the blood pressure usually remains unchanged.

Systematic training and professional selection considerably cut down the   /47
frequency and intensity of such phenomena. In addition, at the present time the techniques of descending to great depths have been worked out in great detail so that the pathological phenomena have been considerably reduced.

Table 9 shows the rate of pressure increase for divers descending in water.

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The changes in atmospheric pressure make themselves felt when entering and leaving the caisson. To avoid any problems with the health of the workers, the period of time spent in the air locks is regulated according to Table 10.

TABLE 9. CHANGE IN RELATIVE RATE OF INCREASE IN PRESSURE DURING UNIFORM DESCENT TO A DEPTH OF 100 METERS IN 5 MINUTES

Duration of the dive (in min.)	Depth of descent (in m)	Absolute pressure (in atm)	Increase in pressure (in atm)	Relative rate of increase in pressure	
0.5	0-10	1-2	1	100	
1.0	10-20	2-3	1	50	
1.5	20-30	3-4	1	33	
2 0	30-40	4-5	1	25	
2.5	40-50	5-6	1	20	
3.0	50-60	6-7	1	16.6	
3.5	60-70	7-8	1	14.3	
4.0	70-80	8-9	1	12.5	
4.5	80-90	9-10	·1	11.1	
5.0	90-100	10-11	1	10	

TABLE 10

Additional pressure (in atm)	Time spent inside the caisson (in minutes)	Additional pressure (in atm) decreases	Time of emergence of workers from caisson (in min)
up to 1	5	from 1 up to 0	5
up to 2	8	from 1.33 up to 0	10
up to 3	10	from 1.66 up to 0	20
up to 4	12	from 2 up to 0	45
		from 4 up to 0	60

At the very beginning of the dive, the saturation of the organism with atmospheric gases increases. Oxygen enters into the general balance of the oxygen metabolism and nitrogen, as an indifferent gas, is distributed in various tissues; it accumulates most of all in the fatty tissue, since its solubility in the latter is 5.24 times greater than its solubility in the

blood. However, this tissue is only slightly vascularized, and therefore the nitrogen begins to accumulate in other tissues first. In a 70 kg man's organism, under normal pressure, about 1,000 cm^3 of nitrogen is dissolved; about 39 cc of this is in the blood. According to the data of Haldane, for each atmosphere of excess pressure a man absorbs about 1 liter of nitrogen, about 70% more than an equivalent amount (by weight) of blood can absorb. This excess is distributed throughout the tissues; the saturation intensity varies markedly in various parts of the organism. Haldane et al., assumed that all parts of the organism are at least half saturated within one hour. However, the experiments of Campbell and Hill (1933) showed that saturation of fatty tissues with nitrogen occurs much more slowly, so that the saturation of the organism lasts for the entire period of time spent in the caisson.

Attention began to be directed a long time ago to the changes that occur in the blood of caisson workers (N. S. Sviontetskiy, 1899; A. S. Solovtsova, 1914; A. A. Gushcha, 1913 and others). As a rule, a decrease was found in the number of erythrocytes and the amount of hemoglobin. Caisson anemia was initially attributed to unfavorable working conditions in the caissons, but experiments on animals and in a pressure chamber showed this change to be correlated with an increase in atmospheric pressure in the pressure chamber. With an additional 10 atmospheres, the number of erythrocytes drops by 900,000 and in some cases by 1,500,000-2,000,000; hemoglobin may drop 24%. The decrease in these parameters occurs because of the deposition of the blood (B. I. Kadykov, Ye. I. Lyubimova, 1936) and the breakdown of the erythrocytes, as indicated by the significant increase in the amount of bilirubin and urobilin. N. S. Solun and R. A. Dymshits (1935), studying the blood of caisson workers who were building a bridge in the vicinity of Saratov, observed an increase in the sedimentation rate in the majority of caisson workers both during an /48 individual descent and following a 3-month period of work under pressure. L. S. Rozanov (1941) confirmed these data and linked them to an increase in the oxygen content of the blood; in his opinion, the latter influences the agglutination capacity of the erythrocytes.

It was noticed a long time ago (V. V. Pashutin, 1881 and others) that an increase in pressure causes a slowdown of cardiac activity and a drop in blood

pressure. A number of changes were also observed in the functions of the organism, but they were not so marked and not so closely linked to hyperbaria.

The time spent in the caisson is regulated by work safety rules. According to a resolution of the USSR People's Commissariat of Labor in 1930, when working at pressures up to 1.8 ata[2] for 24 hours, the total duration of the stay under pressure was set at 7 hours; up to 2.5 ata, 6 hours; up to 3 ata, 5 hours; up to 3.5 ata, 4 hours and above 3.5 ata, 2 hours (cited in M. I. Yakobson, 1950). This does not apply to amateurs and sportsmen; the famous underwater researcher Jacques Yves Cousteau has spent whole days in his marine devices.

As we have already pointed out, Boyle was the first (1662) to observe gas bubbles during decompression. However, it was only Bert (1878) who determined the essential nature of decompression disease, linking it with embolism. He not only established this fact as the reason for the disease, but also studied the chemical composition of the gas bubbles; he found that they consist primarily of nitrogen. Later, decompression disease was studied by many researchers; a particularly important contribution in this respect was made by Haldane et al., Behnke et al., and in the Soviet Union by the school of L. A. Orbeli (Ye. M. Kreps, S. I. Prikladovitskiy, M. P. Brestkin et al.).

It was noticed that the disease usually does not occur during decompression, but afterward, so that it was proposed to call it post-decompression disease. It takes different forms and varies in terms of the degree of seriousness. This is a function of the nature of desaturation during decompression as well as the condition of the organism.

Nitrogen is excreted through the lungs, to which it is transported by the blood. On this basis, we can easily calculate the time required to eliminate the nitrogen during decompression.

Let us use the example of a 65 kg man during decompression from 3 atm to normal pressure. At a normal pressure of 760 mm Hg and a temperature of 37°,

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[2]ata or ati is the pressure in technical atmospheres (kgs/cm^2). 1 ata = 1 kgs/cm^2 = 735.6 mm Hg.

1,000 ml of blood contain 1.2 ml of dissolved nitrogen. This amounts to 1.2 × 65 = 770 ml for the entire organism. When the pressure rises to 3 atm, this will equal 770 × 3 = 2,310 ml; when the pressure returns to normal the organism will have to get rid of 2,310 - 770 = 1,540 ml. The pulse volume is 4,000 ml/minute; each 1,000 can give off 1.2 × 3 - 1.2 = 2.4 ml; 4,000 will give off 2.4 × 4 = 96 ml/minute. The number of minutes required to get rid of the nitrogen will be 1,540:96 = 164.

However, in reality, as we mentioned earlier, the process of gas saturation and desaturation is more complex. Desaturation can occur not only through diffusion and transport, but also through the transport of small bubbles which do not pose an obstacle to circulation (M. I. Yakobson, 1950). Caisson disease does not develop at pressures up to 1.25 ati, even with 100% saturation of the organism. Nitrogen bubbles do not form if decompression begins at a total pressure of 2.5 ati; on this basis, by dropping the pressure by half, the same amount of nitrogen can be eliminated, regardless of the magnitude of the original pressure (J. Haldane and J. Priestley, 1937). From /49 this it follows that a rapid change in pressure from 4 to 2 atmospheres or from 6 to 3 atmospheres will be as safe as from 2 to 1 atmosphere. This has been confirmed by experiments and put into practice in the form of "graduated" decompression.

Even after decompession, small nitrogen bubbles which have not been eliminated may combine to form larger ones and produce an embolus. A radical method of treating decompression disease is therapeutic recompression; it is recommended that the pressure be raised to the level existing in the caisson. However, the frequent cases of relapses of caisson disease indicate insufficiency of pressure and periods of treatment in the methods employed (M. P. Gramenitskiy, 1967; V. Ya. Nazarkin and I. P. Yunkin, 1969). This is particularly true of the serious forms of the disease. The most serious disruptions were observed by G. A. Lavrova (1969) in an experiment on rabbits at 10 ata with rapid decompression; she noticed paralysis as the most frequent symptom of decompression problems.

Bert (1878) found that breathing oxygen during recompression increases its therapeutic effect, and this was subsequently confirmed on many occasions.

However, one must always keep in mind the toxic effects of oxygen (see the section entitled "Hyperoxia"). Therapeutic recompression is only used when working in caissons at pressures above 1.5 ata. Emergence from the therapeutic airlock takes place more slowly than during ordinary locking: 5 minutes for every 0.1 ata and in serious cases 10 minutes for each 0.1 ata; at 1.8 ata, the breathing of oxygen is recommended.

Barotrauma

Barotrauma arises when the atmospheric pressure changes rapidly, either increasing or decreasing, or when there are rapid variations in pressure. This can take the form of local or general changes in the organism. The changes in atmospheric pressure are particularly evident in the tympanic cavity and the inner ear during both hyperbaria and hypobaria. Pronounced changes in atmospheric pressure cause hyperemia and internal hemorrhaging and can even cause rupture of the eardrum, with external hemorrhaging. The experiments of K. L. Khilov and A. P. Smirnov have shown that the eardrum can be traumatized when the pressure in the auditory canal rises by 1.3 atm.

The accessory sinuses of the nose are less sensitive to barotrauma, but changes do occur in them when the atmospheric pressure changes, taking the form of hyperemia and hemorrhaging; preliminary hypoxia and other pathological phenomena intensify them (A. D. Gurkov, 1941).

Even a slight increase in pressure in the lungs causes their distention and passage of air through the alveolar wall into the pleural cavity (Kronneker, 1909; Kats, 1909; cited in J. Haldane and J. Priestley, 1937). Chillingworth and Hopkins (1920) showed that an increase in the intrapulmonary pressure causes a sharp decrease in the arterial pressure in the greater circulation. Polack and Adams (1932) found that at an intrapulmonary pressure of 80 mm Hg, cessation of blood flow to the lungs can occur within 10 seconds, leading to a significant drop in the total arterial pressure. When the pressure in the lungs rises above 80-100 mm Hg, rupture of lung tissue may occur, causing hemorrhaging through the trachea. The organs in closed cavities do not suffer so much from a rapid change in atmospheric pressure.

The effect of atmospheric shock waves on the organism are studied in detail in Chapter 4.

Effect of Reduced Partial Pressure of Oxygen on the Organism

The influence on the organism exerted by air at great heights was noticed even before the discovery of atmospheric pressure.

However, only Bert (1878) finally established that the partial pressure of oxygen is of critical importance in the pathological effect of atmospheric pressure, both when it decreases and when it increases. Following these classical studies, the role of atmospheric pressure as such fell more and more into obscurity as far as slow effects ware concerned. Through the studies of Mosso (1898), the school of Pflueger (Zuntz, Loewy et al., 1905), Barkroft, Haldane and in Russia I. M. Sechenov, his pupil V. V. Pashutin and his associates (P. M. Al'bitskiy, M. Zhirmunskiy and others), the pathological phenomena involved in oxygen starvation were clarified to a significant degree.

The partial pressure of oxygen amounts to approximately 1/5 of total atmospheric pressure (159 mm Hg at sea level). Its variations over a short period of time, involving either a decrease or an increase within narrow limits, do not produce pathological changes in the organism. A drop in the partial pressure of oxygen to 125 mm Hg during prolonged exposure and physical stress causes oxygen insufficiency or oxygen starvation in healthy human beings. Both of these terms have frequently been criticized; it would be more appropriate to use the term "hypoxia", which is the one most frequently employed at the present time.

It was Jourdanet (1875) who was the first to test the effects of oxygen insufficiency on himself during a trip in the mountains of Mexico, where he compared this condition with anemia, and by analogy with anemia called it anoxemia. This term is still used to refer to a shortage of oxygen in the blood. An inadequate supply of oxygen to the tissues has come to be called anoxia. Barcroft (1920, 1937) proposed that it be divided into three basic groups: the anoxic type, in which the arterial blood is insufficiently saturated with oxygen; the anemic type, in which the oxygen capacity is abnormally small in conjunction with a decrease in the blood hemoglobin; and the ischemic type, in which the amount of circulating blood is reduced. Peters and Van Slyke (1931) proposed a fourth type of anoxia -- the histotoxic variety; an example of the latter is poisoning with cyanide compounds, in which the ability

of the tissues to utilize the oxygen conveyed to them is reduced. It has frequently been pointed out that this addition is scarcely justified, since in the latter type of anoxia the oxygen content of the blood is within normal limits. At a conference on hypoxia (Kiev, 1948) the term "anoxia" was criticized on the basis of the fact that in most cases it is hypoxia and not anoxia which is involved in various pathological processes; anoxia is characteristic of clinical death, when oxygen ceases to enter the organism from the environment. At this same conference, a slightly modified classification was adopted:

1. Hypoxic hypoxia: a) from a decrease in the partial pressure of inspired oxygen; b) as a result of impediment of the access of oxygen to the blood through the respiratory pathways; c) due to disturbance of breathing.

2. Hemic hypoxia: a) the anemic type; b) hypoxia with inactivation of hemoglobin.

3. Circulatory hypoxia: a) stagnant forms; b) ischemic forms.

4. Tissue hypoxia. /51

N. N. Sirotinin and F. Ya. Primak proposed that still another type of hypoxia be added -- as the result of a decrease in the permeability of the hemato-parenchymatous barrier, which necessarily leads to a limitation of the diffusion of oxygen in the tissues. However, it was decided to postpone this until new data had been accumulated. Subsequent data confirmed the advisability of establishing this type of hypoxia (V. G. Vogralik and others).

Luft and Finkelstein (1968) suggested the following classification.

Hypoxidation	Hypoxidosis
Hypothermia	Hypoxia
Hibernation	Distribution of enzymatic functions
Hypothyroidism	Shortage of energy resources
Hypokinesia	Accumulation of metabolites

Although hypoxia of all types may have an extremal nature, in this section we shall discuss only hypoxic hypoxia caused by a drop in the partial pressure of inspired oxygen, which develops only under pressure-chamber conditions and the breathing of gas mixtures impoverished with respect to oxygen, since in this type of hypoxia extremal states are a subject of study primarily in aerospace medicine.

Bert (1878) was the first to study the problem of the influence of hypoxic hypoxia on the organism within the scope of comparative physiology, with respect to both phylogenesis and ontogenesis. The data which he collected in this area were not sufficiently numerous that he could draw any significant conclusions. However, it is evident that animals that are less developed in terms of phylogenesis as well as ontogenesis are more resistant to hypoxia.

Further studies supplemented these data. N. N. Sirotinin (1940) investigated the survival of representatives of various classes of invertebrates and vertebrates, placing them in a pressure chamber where the atmospheric pressure was dropped to 60 mm Hg for 45 minutes (approximately 12 mm Hg partial pressure of oxygen). All of the invertebrates used in the experiment (infusoria, hydra, earthworms, medicinal leeches, wood lice, flies, mollusks) withstood this degree of hypoxia without any pathological changes and remained alive without showing any variations from the norm. Poikilothermal vertebrates (goldfish, frogs, axolotls, newts, lizards, agema lizards, "zheltopuziks"[3], grass snakes, runners, desert tortises) proved to be less resistant to hypoxia, but they withstood a reduced atmospheric pressure of 80 mm Hg for 3 hours; only 2 out of 6 axolotls died.

Among homoiothermal animals, representatives were studied from the class Aves (pigeons, chickens, canaries, sparrows and one "mouse-eater"[4], as well as mammals (hedgehogs, moles, bats, laboratory mice and rats, guinea pigs, hamsters, ground squirrels, rabbits, skunks, martens, bears, cats, dogs, wolves, goats, sheep, pigs, donkeys, seals, monkeys). The pigeons proved to be most resistant; they were quite similar to *Columbia livia*, which inhabit rather high--altitude areas in the mountains under natural conditions. The lowest resistance, as was in the case of Bert's experiments, was noticed among the canaries, apparently this is due to hypodynamia resulting from prolonged confinement in cages. Among the mammals, the most resistant were the pigs; it was

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[3]Translator's note: "Yellow-tummy", *Ophisaurus atogus* -- European lizard similar to American glass snake.
[4]Translator's note: The bird *Eaccidger bagius*.

only at a pressure of 370 mm Hg that they developed spasms. It has been known for a long time that cats are relatively less resistant to hypoxia; they developed symptoms of altitude sickness at pressures of 230-260 mm Hg, but they perished at 200-180 mm Hg and sometimes at 160 mm Hg, i.e., at almost the same level as the majority of mammals. It might be thought that seals would be distinguished by considerable resistance to hypoxia, since they are able to stay under water for a long time (15 minutes), but under conditions of hypoxia in a pressure chamber a seal behaves the same as the majority of other mammals. Evidently the adaptational mechanism developed in the course of evolution for diving proved to be useless in a pressure chamber.

The resistance of a human organism to hypoxia can be evaluated on the basis of an analysis of accidents that have occurred during high-altitude flights in open cabins. In 1874, Croce-Spinelli, Sivel' and Tissand'ye ascended in the balloon "Zenit" to an altitude of 8,600 meters. Nobody knows how long they stayed at that altitude, although they began breathing oxygen at an altitude of 4,300 meters, but at some great altitude they apparently stopped using it. As a result, Croce-Spinelli and Sivel' died but Tissand'ye returned to the ground in a deep faint. This flight was of great interest to physiologists, especially Bert, in whose laboratory the balloonists prepared for their flight. I. M. Sechenov and V. V. Pashutin calculated the atmospheric pressure at which the deaths of the balloonists took place. V. V. Pashutin (1881) wrote that man loses consciousness before the partial pressure of oxygen drops to 1/3, i.e., when it is 53 mm Hg instead of 159 mm Hg; in his opinion, the death of the balloonists took place when the atmospheric pressure had fallen by 2/3, i.e., to 260 mm Hg.

In 1934 the German balloonists Jerenk and Mazukh ascended in the sub-stratospheric balloon "Bark von Ziksfel'" to 11,000 meters. Despite the fact that they had the opportunity to use oxygen, they came down dead in the Soviet Union. A. I. Abrikosov, who examined their bodies, could not find any physical injuries but did discover a number of clear signs of asphyxia.

More precise data were obtained on the basis of "high altitude flights" in a pressure chamber. Haldane and Kellas "ascended" in a pressure chamber to 7,500 meters (320 mm Hg); they had great difficulty working the control panel

and following the second hand. At 300 mm Hg they developed symptoms of sig-
nificant mental disturbances. The researchers remained at an "altitude" of
7,500 meters for about 1 hour; one of them did not notice that he had entered
a semiconscious state; the other, observing him, merely smiled, paying no
attention to the fact that his teacher was feeling poorly.

Christensen and Krogh suggested that pilots be tested by making them
breathe air that was impoverished with respect to oxygen in a device that was
a modified Krogh apparatus. The tests continued until the psychomotor function
became weak or dangerous symptoms appeared: a rapid drop of the pulse and
arterial pressure or a disruption of cardiac activity. This usually occurred
when there was about 7% oxygen left in the inspired air.

The Henderson-Pierce device was built using this same principle; it is
particularly widely used in America, but is less accurate than the Christensen
and Krogh apparatus. Flack (1917) suggested that this apparatus be used for
determining the "ceiling" of a pilot; it resembled the above but was less
cumbersome. P. I. Yegorov and A. F. Aleksandrov built an E-A instrument in
1931, which was similar to some extent to Flack's apparatus. The E-A instru-
ment is widely used in the Soviet Union not only for aviation but also for
sports medicine.

A second method of testing resistance to hypoxia is a test in a pressure   /53
chamber. Initially these tests were performed with great care. In the course
of 10 minutes, the pressure was dropped to 535 mm Hg, corresponding to an
altitude of 3,000 meters. In the course of 10 minutes spent at this "altitude",
subjects were examined and then brought to "altitudes" of 4,500 and 6,000
meters. Staying for 10 minutes at an "altitude" of 6,000 meters does not pro-
duce serious problems with the psychic and motor functions, but evan a slight
further rarefaction rapidly produces problems in higher nervous activity.

V. V. Strel'tsov (1938) and his group of associates carried out research
in a pressure chamber, initially on himself and then in 1932 on several
thousand "subjects", pilots and parachutists; the "ascents" in the pressure
chamber extended from 1,000 to 9,000 meters.

Gradually the "ceiling" in the pressure chamber rose. N. N. Sirotinin
(1937, 1938), after drinking the juice of 15 lemons in sugar syrup, "ascended"

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to an "altitude" of 8,000 meters. He continued to feel comfortable, but at about 8,500 meters he becam to develop dangerous symptoms: cyanosis, perspiration, twitching of the extremities, and loss of consciousness. In a second experiment with stimulation of hemopoiesis, Sirotinin "ascended" to an "altitude" of 9,750 meters.

Loss of consciousness in acute hypoxia is the most reliable criterion for establishing the altitude "ceiling"; further "ascent" may pose a danger to life, but this test is not dangerous in a medical experiment, with personnel manning the chamber. N. N. Sirotinin and others later used this method repeatedly to establish a "ceiling". According to the data of N. N. Sirotinin (1939), in most cases consciousness is lost at an "altitude" of 7,000-8,000 meters; individuals can reach a "ceiling" of 9,000 and even 9,300 meters. G. Ye. Vladimirov and his associates (1939) observed syncopal states in a pressure chamber at "altitudes" from 7,000 to 9,000 meters. N. A. Agadzhanyan, A. G. Kuznetsov and V. V. Parin (1968) observed an "altitude ceiling" in persons who had stayed in the mountains at altitudes of approximately 5,200 meters, from 5,000 to 8,200 meters; also in mountain climbers who had ascended to 7,000 meters, from 6,800 to 9,100 meters.

During the second British expedition to Mt. Everest in 1922, the mountain climbers reached an altitude of 8,230 meters. Summerwell climbed to 8,200 meters without using oxygen.

On the basis of this report, J. Haldane, in his paper delivered at the meeting of the British Association in 1926, stated that these data were of enormous significance. He showed that acclimatization can make it possible to reach such altitudes where a non-acclimatized man would surely die.

The highest "ceiling" was reached by Indians -- natives of Marokoch (4,500-5,000 meters above sea level) who do heavy work at this altitude. They could withstand an "altitude" of 11,500 meters for an average of 96 ± 6 seconds; at an "altitude" of 12,000 meters, they did not lose consciousness for 88 ± 1 second. Untrained persons could reach this degree of tolerance only after 6 weeks of acclimatization at an altitude of 4,500 meters (Velasquez, 1959). Persons working in different occupations, carrying out different kinds of physical exercise, develop different degrees of tolerance to hypoxia.

A. F. Aleksandrov and P. I. Yegorov (1939) carried out comparative tests in this regard among athletes and soldiers. The best results were found in a group of runners and the worst results in a group of weight-lifters.

The average maximum attainable altitude of "ascent" in a pressure chamber was the following (in meters):

Runners	8,333	Gymnasts	7,859	/54
Players of various sports	8,220	Rowers	7,800	
Heavyweight athletes	8,064	Soldiers	7,766	
Swimmers	8,012	Pilots	7,714	

N. N. Sirotinin observed the highest "ceiling" (9,300 meters) in mountain climbers who were at high altitudes; the next came swimmers and divers. Pilots, as was the case in the work of A. F. Aleksandrov and P. I. Yegorov, proved to be less resistant to hypoxia; this is evidently due to the fact that they use oxygen during high-altitude flights. An important role in resistance to high altitude is played by the constitution of the individual; persons with a well--developed chest are somewhat more resistant.

Age is important, too. It has been known for a long time that the newborn can withstand asphyxia better than adults; they can remain in a state of asphyxia for 15 minutes, while adults will only last 3-5 minutes. The increased resistance of newborn animals to a shortage of oxygen was observed by Bert (1878); this has been confirmed by many authors, particularly N. V. Lauer, who presented the available material on this question in her monograph (N. V. Lauer, 1959). Later, this age resistance to hypoxia increases; it increases again during maturity and drops off with old age (A. Z. Kolchinskaya, 1964).

Various diseases, particularly those affecting the heart and lungs, decrease resistance to oxygen insufficiency. Schizophrenia, particularly in the form of catatony, increases resistance to hypoxia.

In pressure chambers, such patients have "ascended" to "altitudes" of 10,500 meters without losing consciousness or showing any other dangerous symptoms; catatonics at high "altitude" usually lost their inhibitions. Further ascent was not carried out due to the danger of a rapid development of dangerous symptoms (S. D. Rasin, A. Z. Kolchinskaya, 1952).

Hypoxia develops as the partial pressure of oxygen drops as a function of the duration of exposure. The degree of hypoxia can be evaluated on the basis of the oxygen tension and the percentile saturation of the blood with oxygen, as well as from the state of the organism. The graph shows the dependence of the percentile saturation of the blood with oxygen on the atmospheric pressure and altitude (Figure 8).
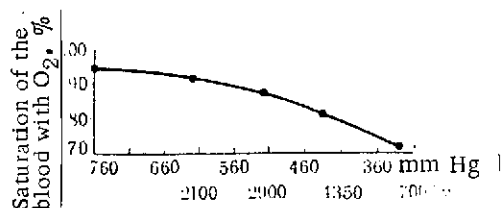

Figure 8. Saturation of the Blood with Oxygen as a Function of Atmospheric Pressure and Altitude.

Normal saturation of the blood with oxygen is between 96 and 98% (Ye. M. Kreps, 1959), but there are considerable individual variations. Percentile saturation of the blood with oxygen during hypoxia under pressure-chamber conditions and while breathing gas mixtures impoverished with respect to oxygen has been confirmed by many authors. Kreps (1959) provides a descending curve of saturation of the arterial blood with oxygen with a gradual "ascent" in a pressure chamber (Figure 9). Breathing oxygen at an "altitude" of 5,000 meters immediately produces an improvement in the percentage of saturation.
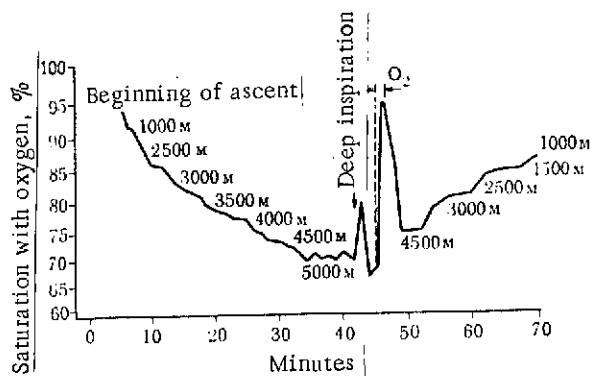

Figure 9. Saturation of Arterial Blood with Oxygen During a Gradual Ascent in a Pressure Chamber (Ye. M. Kreps).

Ye. A. Kovalenko (1962) compared the data of Kreps with his own with respect to determining the oxygen tension in the brains of dogs by the polarographic method, using exposed platinum electrodes which make it possible to express the voltage in percentage of the original oxygen tension on the ground. He also used data on the partial pressure of oxygen in the alveolar air, provided by G. P. Konradi and G. Armstrong. The

results obtained are shown in Table 11.

TABLE 11. COMPARATIVE DATA ON AVERAGE OXYGEN SATURATION OF THE BLOOD AND
OXYGEN TENSION IN THE TISSUES OF THE BRAIN AT VARIOUS ALTITUDES

Saturation of blood and tissues with oxygen	Altitude in kilometers												
	0	1	2	3	4	5	6	7	8	9	10	11	12
Barometric pressure (mm Hg)	760	674	596	525	462	405	353	307	256	230	198	169	144
Partial pressure of oxygen in the alveolar air (mm Hg)	105	90	70	62	50	45	40	35	30	25	20	10	8-5
Saturation of hemoglobin with oxygen (%)	98	97	94	92	85	80	76	68	60	40	29	15	10-5
Degree of saturation of hemoglobin with oxygen (% of original level)	100	99	96	94	87	82	77.5	69.5	61	41	29.5	15.5	10-5
Oxygen tension in the cerebral cortex (% of original level)	100	98	97	88	83	75	70	65	59	55	49	47	39
Oxygen tension in the subcortex of the brain (% of original level)	100	96	91	89	76	69	63	56	50	44	39	36	23.5

In separate experiments the author simultaneously recorded the polarogram
and the electroencephalogram. He observed the development of clearly pro-
nounced high-amplitude slow waves beginning at an "altitude" of 7,000-8,000
meters. At this time, the oxygen tension in the cortex and subcortex of the
brain was 68-50%. At an "altitude" of 9,000-10,000 meters, the slow oscil-
lations predominated but the number of high-frequency oscillations gradually
decreased; the oxygen tension in the cortex and subcortex was 50-40%. At an
"altitude" of 11,000-12,000 meters, the bioelectrical activity of the brain
gradually died out. This was particularly clearly evident at an "altitude" of
12,000 meters, when the oxygen tension dropped to 39-24% of the original level.

No strict relationship between the degree of decrease in oxygen tension in /56
the tissues of the brain and functional disturbances was observed. As we can
see from Table 11, the relative saturation of the blood with oxygen up to
8,000 meters exceeds the oxygen tension in the tissues of the brain, but at

high altitudes it becomes less than in the tissues of the brain. Kovalenko suggests that up to an "altitude" of 8,000-9,000 meters, diffusion of oxygen takes place from the blood into the tissues, while at high altitudes diffusion works in the opposite direction and deoxygenation of the brain takes place, e.g., at an "altitude" of 8,000-9,000 meters, and sharply pronounced symptoms of hypoxic disturbances begin to make their appearance.

V. A. Berezovskiy and I. F. Sokolyanskiy (1965) used polarography to study oxygen tension in the trigeminal muscle of the human arm during an "ascent" in a pressure chamber. The beginning of the decrease in oxygen tension was detected at an "altitude" of 400-600 meters; at an "altitude" of 2,200 meters it amounted to 86 ± 1.7% of the original level; at an "altitude" of 4,200 meters, it reached 64 ± 1.5%.

These facts agree with data obtained under mountain conditions. Thus, at an altitude of 2,100 meters in the mountains, saturation of the blood with oxygen is at the lower limit of normal. Slight muscular activity in the form of twelve deep knee bends/minute decreases this value below normal, and below the levels that are obtained in such cases near sea level. Life is constantly beset with slight physical stresses (except for sleep), so that slight hypoxia develops at altitudes such as 2,000-2,200 meters. A. Z. Kolchinskaya (1963) incorrectly referred to this state as latent hypoxia[5]. This shows up as an excited state, increased garrulousness, a tendency toward laughter, gesticulation, etc. In the mountains, this is more pronounced than under pressure--chamber conditions, due to the longer action of oxygen insufficiency. A great many tests have been carried out involving higher nervous activity by means of various methods, both in the mountains and in a pressure chamber.

In general, at low altitudes (2,000-3,000 meters) disturbances of internal inhibition usually become evident (differentiation, conditional inhibition),

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[5]Latent hypoxia, i.e., hypoxia without hypoxia, is a formulation which lacks logic. In general, without hypoxia of the organism as a whole, there may be partial hypoxia of individual organs and even parts of them. Examples of this are infarct, particularly myocardial infarct, thrombosis of the vessels of the extremities, migraine, etc.

which are considerably intensified at high altitude. The magnitude of the conditioned reflex usually decreases, becoming nonconstant and varying within rather wide limits; adaptation shows inertia of the stimulatory process and weakness of the inhibitory process; there are disturbances of the second signal system and a tendency toward perseverance. At still greater altitudes (5,000-7,000 meters and up) diffuse inhibition and disturbance of consciousness may develop, taking the form of irrational acts, and further ascent can lead to a loss of consciousness. Very early, even at an altitude of 2,000-3,000 meters, disturbances of motorics can be seen; at an "altitude" of 1,000 meters and up the subject begins to make circular movements at times (N. N. Sirotinin, 1954, 1955).

A. Z. Kolchinskaya (1963) suggests that the course of acute hypoxic hypoxia be divided into four stages: 1) latent hypoxia; 2) compensated hypoxia; 3) acute hypoxia with incipient decompensation; 4) uncompensated hypoxia. However, in reality it is not possible to draw a sharp line between these stages; usually the individual variations are quite pronounced as far as resistance to hypoxia is concerned, so that numerous deviations from this system can be observed. In addition, this classification system fails to take /57 into account the rate of ascent, which affects the degree of hypoxic disturbance.

The classification of the acute degrees of hypoxic states is helpful when developing diagnostic machinery for determining the depth of hypoxia, for the purpose of preventing accidents through automatic administration of oxygen (V. B. Malkin, 1963).

Henderson (1933) and Van Slyke (1935) described four degrees of hypoxia when breathing air, impoverished with respect to oxygen. The first degree develops when breathing air at a partial pressure of oxygen of 120-90 mm Hg. This corresponds to an altitude of 4,877 meters. The partial pressure of oxygen in the arterial blood is 60-45 mm Hg, but the saturation of the arterial blood with oxygen is 89-85%; this causes development of headache, weakening of the functions of the central nervous system, disturbance of the coordination of movements, speeding up of the pulse and respiration. The second degree occurs with a drop in partial pressure of oxygen in the inspired air to 70 mm Hg

(altitude up to 7,550 meters), saturation of the arterial blood with oxygen
is 87-74%, and the partial pressure of oxygen in the arterial blood is 55-40
mm Hg. Disturbances of motorics are observed, as is a weakening of self-
-criticism, cardiac weakness during muscular efforts, and a state close to loss
of consciousness. The third stage is the drop in the oxygen in the inspired
air to 45 mm Hg (10,500 meters); the percentile saturation of the arterial
blood with oxygen drops to 33 and the oxygen tension in the arterial blood
drops to 40-20 mm Hg; loss of consciousness occurs, with cerebral coma; adminis-
tration of oxygen eliminates this condition. The fourth stage of hypoxia
arises when the oxygen tension in the arterial blood becomes less than 20 mm Hg,
corresponding to an altitude of more than 10,500 meters; a comatose state is
observed, with a sharp drop in respiration; cessation of the latter leads to
death.

V. B. Malkin (1963) also distinguishes four stages in the development of
acute hypoxic hypoxia. In the third stage, according to his classification,
there is a total loss of working capacity as a result of disruption of con-
sciousness, clonic spasms occur and other serious disturbances become evident.
Prompt signalling and rendering of immediate assistance in the form of
emergency administration of oxygen can lead to a rapid disappearance of hypoxic
disturbances. The fourth stage, that of disturbance to respiration and blood
circulation which threaten life, is characterized on the basis of an estimate
of the behavior of various kinds of animals; as a criterion, the symptoms of
saturation of arterial blood with oxygen were used, as well as the nature of
respiration, arterial blood pressure and EEG. The latter was recommended
for indicating incipient hypoxic danger in aircraft crews; the indicator is
the development of slow waves. However, V. B. Malkin feels that one electro-
encephalogram is insufficient to establish the critical period.

N. N. Sirotinin, V. D. Yankovskiy and Yu. F. Gerya (1969, 1970) studied
the dynamics of clinical death in dogs resulting from depressurization, with
subsequent reanimation. The rarefaction was carried out in a small pressure
chamber, with the atmospheric pressure being dropped from 30 to 18 mm Hg in
45 to 180 seconds. In a number of experiments, the oxygen tension, respir-
ation, EKG and EEG were recorded. The latter was the first to disappear soon

after the development of slow waves, then breathing ceased; the heart continued to beat for a short time, and there were rare monophasic contractions prior to its complete stoppage; there was occasional ventricular fibrillation. Death occurred from acute hypoxia complicated by gas embolism.

Adaptation to hypoxia may be active or passive. Active adaptation begins /58 with an increase in pulmonary ventilation and blood circulation; this is followed by an increase in the number of erythrocytes and hemoglobin, starting with their release from the blood deposits, and then as a result of true hemopoiesis. Later still, tissue adaptation occurs.

Pulmonary ventilation can occur at low altitudes but this is frequently related to physical work or some kind of pathological phenomena in the lungs and cardiovascular system. At an altitude of 2,000 meters in the mountains, N. N. Sirotinin (1966) found increased ventilation in half of 30 (and V. V. Turanov and A. Z. Kolchinskaya (1964) in 9 out of 10) non-acclimatized persons. Under pressure-chamber conditions, increased ventilation begins above this level (3,000 meters) and this is explained by the shorter time of exposure to a reduced partial pressure of oxygen. V. V. Turanov and A. Z. Kolchinskaya (1964) and a number of other authors noticed this phenomenon at an "altitude" of 1,000 meters. Pulmonary ventilation can increase because of either the frequency or depth of respiration. In the majority of cases, adaptation through frequency of respiration arises in untrained persons, while in trained individuals it takes place through the depth of respiration.

As the altitude increases, ventilation increases as well. However, it sometimes remains constant or even decreases. This usually occurs when adaptation takes place primarily by virtue of increased blood circulation. In general, these two forms of adaptation are mutually related. At high altitude, respiration takes on a wavelike nature, and is observed more frequently in mature individuals. At an altitude of 4,000 meters or more in the mountains, this phenomenon becomes more pronounced and shows a tendency toward Chain-Stokes respiration; under pressure-chamber conditions, such respiration arises at high altitudes. During sleep, this kind of respiration develops below the 2,000 meter altitude in middle-aged persons, particularly after taking a soporofic (N. N. Sirotinin, 1954).

Increased blood circulation due to speeding up of cardiac activity can develop at the same altitudes as increased respiration. In some persons, adaptation proceeds more on the basis of respiration, while in others it is due to blood circulation. As is the case in respiration, speeding up of cardiac activity usually occurs in untrained persons, while in trained ones adaptation occurs primarily through increased stroke volume of the heart. Speeding up of cardiac activity regularly begins at 2,000 meters and continues to increase slowly up to altitudes of more than 4,000 meters, then develops more rapidly. At an altitude of approximately 5,000 meters and up, pathological phenomena are observed in the form of extrasystole, a decrease in EKG voltage with an increase in the T spike; symptoms of decompensation develop in the form of cyanosis and edema of the extremities; at high altitudes in the mountains, pulmonary edema sometimes develops.

As was shown by Barcroft and Z. Yu. Sabinskiy before him (1865), contraction of the spleen and expulsion of blood from the deposits occurs during anoxia during the initial stages of decreased atmospheric pressure.

It is well known that adaptation to hypoxia takes place due to increased true hemopoiesis; this has been proven by studies of bone marrow punctures, an increased number of reticulocytes and a leftward shift. The degree of increase in the erythrocytes and hemoglobin varies as a function of a number of factors (active or passive ascent, degree and duration of hypoxia, etc.). In general, acclimatization to high mountain climates is always accompanied by an increase in the amounts of erythrocytes and hemoglobin.

In addition, in high-altitude hypoxia, there is a decrease in the number of erythrocytes and hemoglobin. A number of proofs have been provided to support the breakdown of red blood at high altitude and subsequent activation /59 of hemopoiesis by the accumulation of hemopoietins from the erythrocytes that have broken down. N. N. Sirotinin (1970) concludes that the increase in the oxidative surface of the blood during adaptation to hypoxia is not so great that it can satisfy the oxygen demands of the organism to a significant extent; apparently the qualitative changes in hemoglobin and its fractions are of great significance. However, additional studies are required to support this conclusion.

It has been suggested that adaptation to hypoxia also takes place by virtue of changes in the tissues. This problem has not been clarified completely. Undoubtedly the amount of myoglobin in the muscles increases during prolonged hypoxia, especially after muscular exercise, and this may be of adaptive significance. The most convincing proponent of the significance of tissue adaptation is Z. I. Barbashova (1960).

Passive adaptation to hypoxia is particularly clearly evident in the lower animals, in which active adaptation is either absent or only slightly evident. Infusoria begin to move more slowly when there is a shortage of oxygen, then stop. It is true that it is difficult in such cases to decide what constitutes adaptation and what is a consequence of oxygen deficiency. When the partial pressure of oxygen falls, highly organized animals like mice, usually stop moving around actively and sit quietly, as if trying not to make any unnecessary movements. A good example of passive adaptation is hibernation, during which resistance to hypoxia increases markedly (Bert, 1878; N. I. Sirotinin, 1940; N. A. Arkhangel'skaya, 1949).

A. D. Slonim (1962) and his students placed great importance on passive adaptation in adjustment to oxygen deficiency; they stressed the important role of a change in the function of the thyroid gland. P. N. Veselkin (1942), Ye. V. Kolpakov and N. V. Lauer (1949), M. Ye. Vasilenko (1955) and others have observed an increase in resistance to hypoxia following removal of the thyroid gland. This apparently has to do with decreased metabolism as well as decreased oxygen demand. The same phenomenon was observed following removal of the pituitary. P. N. Veselkin (1942), Ye. V. Kolpakov and N. V. Lauer (1949) have described an increase in resistance to oxygen deficiency in hypophysectomized rats. Vacca and Boeri (1953) observed decreased resistance to hypoxia in the same rats. V. B. Malkin and Yu. A. Yurkov (1962) as well as N. A. Roshchina (1968) failed to observe any significant differences in the hypoxic resistance of hypophysectomized animals (cited in I. R. Petrov, 1967).

This difference in the data of various authors may possibly be due to the fact that hypophysectomized animals are very sensitive to various influences which decrease their resistance. On this basis, it is not always possible to determine clearly their true increased resistance to hypoxia. ACTH increases

the resistance of animals to oxygen deficiency. Administration of cortisone, or hydrocortisone, increases resistance to hypoxia (Tabusse et al., 1954). I. R. Petrov and his associates have provided considerable data on the significance of the adenohypophysis and the adrenal cortex in oxygen insufficiency and have established their roles in this pathological process (I. R. Petrov, 1967). Inhibition of the central nervous system also increases resistance to oxygen starvation (I. R. Petrov, 1952).

Administration of various pharmacological substances can increase resistance to hypoxia (N. N. Sirotinin, 1941; V. V. Turanov, 1961; S. Ya. Arbuzov and L. V. Pastushonkov, 1969). Acclimatization to high mountain climates also increases the "ceiling" under pressure chamber conditions (N. N. Sirotinin, 1937, 1938, 1939, 1940, 1966; G. Ye. Vladimirov et al., 1939; N. A. Rossolovskiy, 1951; M. A. Aliyev, R. S. Sultakov, 1966; N. A. Agadzhanyan, A. K. Kuznetsov, V. V. Parin, 1968; P. V. Vasil'yev, V. B. Malkin et al., 1968).

Altitude sickness. Altitude sickness, in the form of mountain sickness, has been known for a long time. Apparently it was recognized for the first time in mountainous areas of Asia, where it had been given native names such as "bis", "tunk", "dam", and "tutek". The population living in the Andes calls mountain sickness "soroche", "veta" and "puna". Mountain sickness was given its name by Akost (1590) who observed it in himself and his comrades in a journey through the Peruvian Andes. As aviation developed, similar symptoms began to be observed during balloon ascents.

Sossure (1786, 1787), studying mountain sickness by climbing Mount Blanc, was the first to explain it by attributing it to the effects of reduced atmospheric pressure and later, following the famous studies of Lavoisier, to a shortage of oxygen. Jourdane (1861) also explained its origin by a shortage of oxygen in the blood -- "anoxemia". However, it was only Bert (1878) who definitely proved that symptoms of altitude sickness are linked primarily to a shortage of oxygen. This point of view was later confirmed by many other researchers.

It has been shown that there is a tendency toward non-gaseous acidosis at moderate altitudes, while ascent to higher altitudes causes development of

alkalosis as a result of hyperventilation. The most characteristic symptoms of mountain sickness coincide with the development of alkalosis (N. N. Sirotinin, 1931-1935). During hypoxia under pressure-chamber conditions, as well as during flights when the reduced partial pressure of oxygen is active for a shorter time, alkalosis is less pronounced.

The pathogenesis of altitude sickness is linked to a number of disturbances in the functions of individual systems and organs: nervous sytem, respiration, circulation, muscles, digestive system, excretory system and endocrine glands. The first symptoms of altitude sickness may develop at low altitudes (1,000-2,000 meters); at these altitudes it develops in persons with problems affecting the organs of respiration, circulation or the blood. In a significant majority of cases the symptoms of altitude sickness develop in the mountains above 3,000 meters, usually at about 4,000 meters and up; under pressure-chamber conditions and during flights, altitude sickness develops at higher altitudes as the result of reduced exposure to oxygen insufficiency.

The disturbance of higher nervous activity is particularly important. This pathological symptom has been studied by Soviet researchers using the conditioned reflex method. Significant changes have been observed in the higher nervous activity of dogs in a pressure chamber, beginning at "altitudes" of 1,000 to 2,000 meters, taking the form in most cases of an increase in reflexes to weak stimuli, brief excitation and even phasal states, which usually arose at high altitudes. G. I. Mil'shteyn (1952), observed that individuals displayed limited inhibition with a slight drop in partial pressure of oxygen (125 mm Hg), which caused a disruption of the ordinary force ratios (development of hypnotic phases). G. V. Altukhov (1955), studying higher nervous activity with simultaneous study of the saturation of the blood with oxygen, found that when saturation dropped to 80-75% there was an increase in the stimulatory process; as hypoxia developed further (up to 60-43% saturation), there was a slackening of the stimulatory process and a gradual increase in the inhibitory process.

It has also been noted that changes occur at high altitudes in the function of other systems as well, particularly the digestive system. The rate at which altitude sickness develops is a function of the rate of ascent and the condition of the organism. The optimum rate of ascent with respect to tolerance

to hypoxia is 150 m/minute; at high rates there is loss of consciousness without pronounced preliminary disturbances; at slower rates, a presyncopal state develops before loss of consciousness. Various diseases, particularly flu and catarrh associated with colds, promote the development of altitude sickness.

The development of mountain sickness involves other factors besides oxygen insufficiency -- physical fatigue, chill, ionized air, and ultraviolet radiation. In the case of a rapid ascent by cable car, the conditions for development of mountain sickness differ only slightly from those involved in an "ascent" in a pressure chamber. When making an ascent on foot, physical fatigue always makes itself felt, promoting the development of symptoms of mountain sickness. The symptoms of mountain sickness differ somewhat from those under pressure-chamber conditions: headache, nausea and sometimes vomiting, hemorrhaging from the nose, less frequently from other mucous membranes, rarely loss of consciousness; sometimes the above-mentioned changes in higher nervous activity are more pronounced.

Treatment of altitude sickness consists primarily in bringing the individual down from high altitude; it must be kept in mind in this connection that a rapid descent can cause posthypoxic phenomena which are largely reminiscent of the symptoms of altitude sickness. If descent is impossible, oxygen, or still better, carbogen must be given. In case of mountain sickness it is useful to give acid substances. The treatment is of a symptomatic nature. In order to get rid of the headache and dizziness, it is recommended that phenacetin or acetylsalicylic acid be given, as well as amidopyrin or citrovanillin, or massaging the head; stimulants that can be given include strong coffee and caffein; in case of cardiac weakness, strophanthin should be given. To stimulate the respiratory center, the individual should be given spirit of hartshorn to drink and the upper respiratory pathways should be stimulated with carbonic acid; lobeline or cytitone should be administered.

Prevention of altitude sickness consists primarily of oxygenprophylaxis. Considerable emphasis is placed on adding carbonic acid to the oxygen; this does not have a noticeable positive effect up to altitudes of 13,500 meters, but in the case of mountain sickness, when the carbonic acid level in the blood

increases sharply, such methods of prophylaxis are completely justifiable. Other forms of prevention of altitude sickness are much less effective. Inhabitants of mountainous areas use acid fruits and stimulants to prevent mountain sickness. N. N. Sirotinin suggested that an acid mixture of citric acid in sugar syrup (15 grams of citric acid and 200 grams of sugar) with ascorbic acid added be used to prevent this problem. This mixture was later tested extensively by V. V. Turanov and gave positive results. As was mentioned earlier, ammonium chloride was recommended for the same purpose, as well as other substances (N. N. Sirotinin, 1941; V. V. Turanov, 1961; S. Ya. Arbuzov and L. V. Postushonkov, 1969).

Hyperoxia

As has been established, the atmosphere of the Earth was nearly devoid of oxygen for some time (E. Yuri, 1959; A. Vinogradov, 1959). The accumulation of oxygen in the atmosphere took place slowly, as a function of the development of green plants, and reached its maximum (in the opinion of V. I. Vernadskiy) with /62 the development of the gymnosperms. The data from evolutionary biochemistry indicate that life developed under anaerobic conditions (A. I. Oparin, 1957). The biochemical evolution of the organic world followed a path of increasing complexity and was accompanied by mechanisms of oxidative processes; from anaerobic oxidation to the utilization of the oxygen in the atmosphere, i.e., its respiration. At the present time, this relationship is seen in both phylogenesis and ontogenesis. This view was supported by research indicating significant resistance to oxygen insufficiency among lower animals. The same resistance to hypoxia has been observed in early stages of ontogenesis (Bert, 1878; N. N. Sirotinin, 1940; N. V. Lauer, 1959). One proof of resistance to hypoxia in early ontogenesis due to glycolytic processes is a decrease in this resistance when glycolysis is suppressed by monoiodoacetic acid.

The transition of anaerobic processes to respiration constitutes an accommodation to increased oxygen content in the atmosphere, which is clearly a progressive phenomenon, since life can be supported through respiration approximately 20 times more economically than through glycolysis. However, the processes relating to respiration are evidently more resistant to various influences, particularly a conditioned oxygen shortage (N. N. Sirotinin, 1966).

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In contrast to hypoxia, hyperoxia[6] is not observed to a significant degree in natural conditions, and therefore the animal organism cannot accommodate to it in the course of evolution. However, this adaptation to hyperoxia does exist in the majority of cases, taking the form of reduced pulmonary ventilation, decreased blood circulation, and a decrease in the oxidative surface of the blood and the number of reticulocytes.

Priestley (1774) noted that mice died in pure oxygen; he was the first to demonstrate its toxicity and predict that it could be harmful to human health. Bert (1878) found that oxygen at high partial pressure has a pernicious effect, especially on small animals (birds); he also showed that the blood from animals poisoned in this fashion was not toxic; this has nothing to do with the influence of oxygen on hemoglobin, since the toxicity of the oxygen affects animals that do not possess hemoglobin (insects), as well as plants. Bert described the most characteristic symptom of oxygen intoxication among higher animals -- the development of tonic spasms; he compared them with spasms resulting from strychnine poisoning.

The comparative-physiological studies of Bert on the influence of increased partial pressure of oxygen on the organism made it possible to clarify the pathogenesis of this phenomenon. Later these studies were continued by many other authors (Smith, 1889-1898; S. I. Prikladovitskiy, 1940; N. N. Sirotinin, 1952; A. V. Voyno-Yasenetskiy, 1958, and others). Smith established the local toxic effect of oxygen on cells adjacent to the air passages and not so well protected against the direct influence of oxygen as the cells of the internal organs. Mice that were placed in 0.8 atm pure oxygen died in 4 days, while at 1.25 atm they died in 64 hours, and still earlier at higher partial pressures of oxygen. Death was the result of the pneumonia which developed. These data were confirmed by a number of authors (N. V. Lazarev, 1941; A. G.   /64
Zhironkin, A. F. Panin, P. A. Sorokin, 1965).

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[6]At a conference on oxygen therapy and oxygen insufficiency (1950), N. N. Sirotinin proposed that this term be used to represent the state opposite to hypoxia.

These experiments were performed on representatives of various classes of vertebrates: mammals, birds, reptiles, amphibians, fish and various representatives of the invertebrate kingdom. It was found that different animals possess different degrees of sensitivity to the toxic effects of oxygen; animals with a high intensity level of metabolism, and smaller size, die more rapidly than animals with a lower level of metabolism. On the other hand, rats turned out to be less resistant than mice; old rats were less resistant than young ones.

It is interesting that in ontogenesis the resistance to hyperoxia decreases in the same fashion as hypoxia. S. I. Prikladovitskiy (1936) studied the reaction of mice of various ages to increased oxygen pressure. A group of newborn mice (from birth up to 12 days) tolerated 2 days exposure to 8 atm oxygen, showing no toxic spastic phenomena. A group of mice aged 13 to 22 days proved to be more sensitive than the next group, the fully adult mice. N. N. Sirotinin (1952) confirmed the data of S. I. Prikladovitskiy and directed attention to the fact that resistance to oxygen corresponds to the situation in hypoxia with respect to both phylogenesis and ontogenesis. However, this relationship is more clearly pronounced only in the case of hypoxia.

I. M. Ivanov, B. D. Kravchinskiy, S. I. Prikladovitskiy and V. R. Sonin (1934) observed that spasms do not result from oxygen in decerebrate animals. A. G. Zhironkin (1940) also failed to observe typical oxygen spasms in decorticized cats, but he did notice a sharply increased general motor excitation; however, he described characteristic oxygen clonic and tonic spasms in decerebrate rabbits. A. V. Voyno-Yasenetskiy (1966) studied the possibility of the development of epileptiform complexes of oxygen poisoning in representatives of various animal classes. He noticed this symptom complex in worms, insects, cyclostomes, fish, amphibians, reptiles and mammals. He found that in various species of animals the nature of the reaction to the effect of increased oxygen pressure was theoretically the same. A. V. Voyno-Yasenetskiy concluded that evolutionary development of functions introduces to the method of reaction only a complication of a form of the external manifestation of the reaction without changing the method itself.

All of these facts speak in favor of the theory of toxic effects of oxygen outlined above. However, Gesell (1923) stressed the previously known fact that

the toxic nature of oxygen is reinforced in the presence of carbon dioxide. He linked this to the fact that when the partial pressure of oxygen is increased by 3 atm or more, all of the blood is saturated with oxygen and hemoglobin is found in the oxyhemoglobin state in both the arterial and venous blood. Since it is a more powerful acid than hemoglobin, oxyhemoglobin is unable to bind the carbon dioxide and therefore to remove it from the tissues. Carbonic acid is therefore accumulated in large amounts and causes tissue asphyxia. I. M. Dedyulin (1943), working with rabbits at a pressure of 3-5 atm of oxygen, observed an increase in the carbon dioxide tension in the tissues up to toxic levels; in addition, the amount of this substance in the blood decreased. It was also found that a carbon dioxide concentration which is harmless at partial pressures of oxygen less than 1 atm becomes toxic at 4 atm oxygen. I. F. Sokolyanskiy (1970), observed the development of spasms in white rats at 4 atm oxygen after 107.4 ± 3.84 minutes, while when carbon dioxide accumulated in the /64 chamber the spasms developed at only 51.6 ± 1.4 minutes.

The comparative pathological data presented above indicate a direct influence of oxygen on tissue metabolism. Lower animals, which do not possess hemoglobin, and especially plants, are also subject to the toxic action of oxygen, which gave Bert a basis for stressing the inhibition of respiration with increasing partial pressure of oxygen. Z. S. Gershenovich and A. A. Krichevskaya (1950) observed inhibition of brain tissue respiration in a Warburg apparatus with increased partial pressure of oxygen. Hence, the toxic effect of oxygen amounts to an inhibition of tissue respiration as well as an accumulation of carbonic acid and its toxic effects on tissues; the latter affect is combined in animals that possess hemoglobin at pressures above 3 atm. Subsequent studies confirm this view. In addition, A. G. Zhironkin (1963) observed that rabbits that have become adapted to hypoxia under pressure-chamber conditions were more resistant to hyperoxia. I. F. Sokolyanskiy observed the same effect in animals acclimatized to high mountain conditions. Hence, adaptation to hypoxia to a certain extent prevents the development of both hypoxia and the toxic effects of oxygen; in other words, an important role is played by hypoxia of the histotoxic variety in the pathogenesis of the latter. As pointed out by V. V. Pashutin (1881), it is possible to assume without too great an error that oxygen becomes harmful to man and other animals when its

pressure rises to 3 times the level found at the surface of the Earth, i.e., above 60-65%. However, oxygen concentrations of 40-45% have also proven to be toxic. Several researchers have noticed the first symptoms of the toxic effect of oxygen at 73% of its content in the inspired air, while most of them observed it at much higher concentrations (83% or more).

Oxygen pressure at 1 ata causes clearly pronounced physiological and pathophysiological changes in the organism. Dohmen (1868) observed that oxygen reduces the depth of inspiration. Mosso (1898) noticed a decrease in the respiration frequency. Campbell (1928), G. I. Zilov (1961) and many others confirmed these observations, but some also noticed an increase in pulmonary ventilation which they viewed as the result of the toxic action of oxygen. A. G. Zhironkin, A. F. Panin and P. A. Sorokin (1965) observed a speeding up of respiration and a decrease in pulmonary ventilation in the majority of healthy persons who breathed oxygen for 4-5 hours. G. A. Vaksleyger (1968) observed the change in the respiration of dogs in chronic experimental conditions under the influence of oxygen inhalation: respiration became biphasal, and the depression by respiratory movements during the first 1-3 minutes was replaced by a second phase involving recovery of respiratory activity (adaptation phase).

Breathing oxygen at 1 ata causes normalization of disrupted breathing in the majority of cases. Thus, in hypoxic hypoxia, periodic respiration of even the Chain-Stokes variety disappears quite rapidly. T. A. Aref'yeva (1968) observed disappearance of the Chain-Stokes breathing under the influence of oxygen in frogs with experimental circulatory hypoxia.

At a pressure of 1 ata, oxygen exerts an influence on the cardiovascular system. In healthy persons and animals, slowing of the pulse was observed in most cases. A. G. Zhironkin, A. F. Panin and P. A. Sorokin (1965) observed that breathing oxygen at 1 ata for 2-5 hours caused pronounced decreases in pulse rate to 6-23 beats/minute in 26 out of 30 healthy individuals. /65

Under the influence of breathing oxygen, arterial pressure changes comparatively slightly and frequently remains constant. A. G. Zhironkin, A. F. Panin and P. A. Sorokin observed a slowing of the blood flow rate in half the cases in healthy persons following two hours of breathing oxygen; they did

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notice, however, a decrease in the volume of circulating blood in such cases. Mention was made earlier of data in the literature on the decrease of the number of erythrocytes and hemoglobin under the influence of oxygen breathing. However, V. B. Farber (1948) was unable to observe any deviations in erythropoiesis in healthy persons who breathed oxygen for 5 hours. Ya. G. Uzhanskiy et al. (1958) found a definite decrease in the number of erythrocytes and the amount of hemoglobin in normal animals under the influence of hyperoxia. The number of reticulocytes decreases when pure oxygen is breathed.

It was mentioned earlier that when animals are allowed to remain for several days in an atmosphere of pure oxygen, pronounced toxic effects develop. N. A. Agadzhanyan (1969) found that exposure of animals for several days to an atmosphere with 89-95% oxygen at normal pressure causes pronounced toxic effects: beginning with the 3rd day, oxygen consumption decreases, the system of relative phosphorylization of brain tissue is damaged, and the general reactivity of the animals is reduced. Exposing the animals for up to 10 days to an atmosphere of pure oxygen at a pressure of 198 mm Hg does not produce any significant changes in the physiological reactions of the organism. On the basis of these and other data, N. A. Agadzhanyan (1968) developed the basis for total pressure and oxygen regimes in aircraft cabins.

The influence of oxygen on the higher levels of the central nervous system at a pressure not in excess of 1 ata for a short time is comparatively slight. However, general excitability of the organism has frequently been observed under these conditions. According to the data of G. V. Zilov (1953, 1955), an increase in the oxygen content to 55% causes increased conditioned reflex activity, while a further increase, to 96%, causes the opposite effect. A. G. Zhironkin, A. F. Panin and P. A. Sorokin (1965) observed decreased conditioned-reflex salivation at 1 ata oxygen in dogs with a predominance of inhibitory processes. G. V. Troshikhin noticed a cessation of conditioned-reflex development in mice kept in an environment of 80% oxygen. N. I. Krasnogorskiy (1934) found a moderate rise in positive conditioned reflexes in children as a result of breathing oxygen. N. N. Sirotinin (1958) studied higher nervous activity at a pressure of 1 ata oxygen in mice, dogs and volunteers; the changes observed under these conditions were nearly normal.

At pressures above 1 ata oxygen, the same trend is observed in the change in functions, but is more pronounced. One is struck by the fact that the first symptoms of toxic action of oxygen are accompanied by the same changes in the central nervous system as in hypoxia: decreased attentivity, disruption of coordination of movement, weakness of memory, development of a large number of errors in writing (N. N. Sirotinin, 1958; G. L. Zal'tsman, 1961, 1968; A. G. Zhironkin, A. F. Panin, P. A. Sorokin, 1965).

N. N. Sirotinin (1958) observed disappearance of defensive-motor conditioned reflexes in mice at a pressure of 4 ata; at 5 ata the mice began to die. In dogs, conditioned reflexes developed by the defensive-motor method /66 began to be disturbed at 3 ata; at this point the conditioned reflex was retained, but differentiation was absent; at 4 ata the conditioned reflexes disappeared. In an autoexperiment, N. N. Sirotinin observed at a pressure of 3.47 ata that on the basis of an examination using the "correction" method of A. G. Ivanov-Smolenskiy the latent period of the reaction decreased slightly, its magnitude increased somewhat, and there were disturbances of the differentiation and delayed inhibition; psychomotorics, studied using the Thorndike method, were also disturbed. An examination using the vocomotor method failed to show any deviations from normal.

G. L. Zal'tsman (1968) observed that subjects displayed a decrease in motor reflexes and to a lesser degree a reduction in the magnitude of the delaying reflexes, at a pressure of 3.5 ata; differentiated reflexes were not disturbed at all. A. G. Zhironkin, A. F. Panin and P. A. Sorokin (1965), at a pressure of 2.5 ata, observed an initial speeding up of the rate of reactions to light, with later prolongation, in five subjects; at 2.5-3 ata, they observed a slight narrowing of the field of vision (by 10-14%). Narrowing of the field of vision is a function of the vasoconstrictive effect of oxygen on the vessels of the retina, which occurs in parallel with constriction of the vessels of the brain.

B. D. Kravchinskiy and S. P. Shestovskiy (1936), on the basis of an autoexperiment, feel that it is possible to remain safely at the 4 ata oxygen level for 20 minutes, and at 5-6 ata for up to 10 minutes; this is followed by oxygen poisoning. Three stages of acute oxygen poisoning have been defined:

1) speeding up of respiration and pulse, increase in blood pressure, dilation of the pupils, increased activity with individual twitching of muscles;

2) stage of spasms similar to epileptic, with clonic and tonic symptoms;

3) terminal, with weakening of the spasms and disturbance of respiration, changing to individual inspirations. Death is caused by paralysis of the respiratory center (A. G. Zhironkin, A. F. Panin, P. A. Sorokin, 1965).

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